



DEPARTMENT OF HEALTH & HUMAN SERVICES

AFI-35

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Public Health Service **d14806**  
Food and Drug Administration

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

19900 MacArthur Blvd., Ste 300  
Irvine, California 92715-2445  
Telephone (714) 798-7600

March 13, 1998

WL-20-8

WARNING LETTER

Stephen Brown  
President  
Anabolic, Inc.  
17802 Gillette Avenue  
Irvine, CA 92714

— Dear Mr. Brown:

During an inspection of your pharmaceutical manufacturing facility conducted between February 9 to February 17, 1998, our investigators found significant deviations from the Good Manufacturing Practice for Finished Pharmaceuticals regulations (Title 21, Code of Federal Regulations (CFR), Parts 210 and 211). Such deviations cause human drugs manufactured by your company to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (Act).

Our investigation revealed there is no assurance that the methods used in or the facilities and controls used for the manufacture, processing, packing, or holding of your finished pharmaceuticals are in conformance with the GMP requirements as follows:

1. Failure to establish control written production and process control procedures to ensure proper execution of various production and process control functions [21 CFR 211.100]. For example:
  - Changes were made to several production batch records without the proper approval, approval was not obtained prior to performing changes to the batch production record and changes are not reflected in the master batch record. Additionally, two different control revisions of your Product Quality Control Report were used in the production of Mescolar L.A. T/R without justification.

- Your established procedures do not address how changes will be tracked or referenced in approved documents such as batch records, written procedures, and stability records.
2. Failure to ensure that automatic, mechanical, and electronic equipment, including computer(s) are inspected or checked according to a written program designed to assure proper performance [21 CFR 211.68]. For example, your computer software used for tracking raw material, finished product quarantine/release, and archiving master formulas has not been validated.
  3. Failure of the quality control unit to conduct investigations to determine reason for drug products failing to meet specifications [21CFR211.192]. For example:
    - At least six separate incidences were noted where a product failed to meet the established specifications, the drug product was reworked, and commercially distributed with no assessments conducted to determine whether or not there was sufficient data to support the rework corrective actions taken.
    - Drug products were released without proper approval signatures on the Product Quality Control Reports.
  4. Failure to establish adequate procedures to assure equipment and utensil are sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of drugs beyond the official or other established requirements [21 CFR 211.67]. For example:
    - There are no written procedures that clearly specify how many consecutive lots can be manufactured without major cleaning.
    - Cleaning validation studies do not reflect actual worst case production practices in that the studies were not performed after the maximum number of same product consecutive production runs.
    - There are no written procedures which address how major and minor production equipment cleaning will be tracked and documented.

5. Failure to establish complete manufacturing and control instructions in master production records to assure uniformity from batch to batch for each drug product [21CFR211.186]. For example:
  - Minimum and maximum operating parameters are not specified in Chilonsonor batch production records.
  - There are no written coated tablet weight specifications in the Nephro-Fer Rx Tablet batch record.
6. Failure to establish sufficient laboratory controls to assure that components, in-process materials and drug products conform to appropriate standards of identity, strength, quality and purity [21 CFR 211.160]. For example:
  - A formal investigation was not initiated or documented in reference to incidences of out-of-specification results, only the retest results were reflected in the batch record, no documented rationale for invalidating the initial out-of-specification results, and lack of documented review by Q.C. Laboratory Manager of retesting performed.
  - There is no established written procedure which addresses how secondary standards will be compared to USP primary reference standards.
7. Failure to control your established testing program designed to assess the stability characteristics of your drug products [21 CFR 211.166]. For example, the stability program does not address the following:
  - whether stability samples are representative of the entire production run (i.e. beginning, middle, and end).
  - the number of samples placed on stability.
  - the number of stability samples to be pulled at each test station.

- the manner in which stability samples will be labeled.

Our office has significant concerns about the corrective measures undertaken by your company to eliminate the recurrence of the deficiencies disclosed in earlier inspections conducted by our office. Whereas, many of the current deficiencies are similar to earlier deficiencies found at your company we wish to meet with you and representatives of your company to discuss our concerns. Please contact Kim Childress, Consumer Safety Officer at 714-798-7732 to arrange a meeting and be prepared to discuss your corrective measures at this meeting. We have enclosed a copy of an earlier Warning Letter sent to your company on August 23, 1995.

We acknowledge that you have submitted to this office a response concerning our investigator's observations noted on the form FDA 483. We have completed review of your response; there are several incidences where insufficient information was supplied or do not address our concerns. We will provide our comments regarding your proposed corrective measures at the meeting.

The above listed violations are not intended to be construed as all inclusive of those existing at your firm. It is your responsibility to ensure that all requirements of the Federal Food, Drug, and Cosmetic Act and regulations promulgated thereunder are being met.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Such action includes, but is not limited to, seizure and/or injunction. Federal agencies are advised of the issuance of all warning letters about drugs and devices so that they may take this information into account when considering the award of contracts. Additionally, pending Antibiotic Form 6, NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

You should notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you plan to take to assure that each of the noted violations will be corrected. Your response should also include an explanation of the specific steps which will be taken to prevent the recurrence similar violations.

Your reply should be addressed to:

Dannie E. Rowland  
Compliance Officer  
U.S. Food and Drug Administration  
19900 MacArthur Boulevard, Suite 300  
Irvine, California 92612-2445

Sincerely,

A handwritten signature in cursive script, appearing to read "Elaine C. Messa".

Elaine C. Messa  
District Director

State Department of Public Health  
Environmental Health Services  
Attn: Chief, Food and Drug Branch  
601 North 7th Street  
Sacramento, CA 94234

enclosure